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<b>(54) Title:</b> POLYURETHANE-COATED INTRAVASCULAR PROSTHESES (STENTS) FOR THE TREATMENT OF BLOOD VESSEL STENOSIS  <b>(57) Abstract</b>  A new method to treat blood vessel stenosis using endovascular prostheses which are coated with amphiphilic polyurethanes to which medicines can be coupled. By coating endovascular prosthesis with amphiphilic polyurethanes, we have succeeded in significantly improving the bio- and bloodcompatibility of endovascular prostheses. These amphiphilic polyurethanes have the property, when implanted in human or animal tissue and blood vessels, of remaining stable and seeming not to provoke an inflammatory reaction. Furthermore it is possible to incorporate medicines in these polymers which, after implantation of the polymers, are slowly released at the location of the place of implantation. This system can further reduce the thrombogenicity of the prostheses coated with the polyurethanes and inhibit the rejection against these prostheses.		

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5 POLYURETHANE-COATED INTRAVASCULAR PROTHESES (STENTS) FOR THE  
TREATMENT OF BLOOD VESSEL STENOSES. A new method to treat  
blood vessel stenoses by means of endovascular protheses  
which are coated with amphiphilic polyurethanes to which  
medicines can be coupled.

10 DESCRIPTION

Treatment of blood vessel stenoses by means of a balloon  
catheter is a popular method. Last year, more than  
15 6,000 patients with coronary heart disease were treated by  
this method in our country. The problem with this method is  
on the one hand the danger that a tear occurs during the  
blowing up of the balloon whereby the blood vessel can close  
and thus cause an acute myocardial infarction, on the other  
20 hand it is well documented that this treatment method is  
accompanied by a frequent restenosis of the treated blood  
vessel within 6 months of the treatment. To solve this  
problems, medicines were tested in order to prevent the  
restenosis and furthermore new devices were developed.

25 One of these new methods consist of placing a metal  
intravascular prothesis (stent) at the level of the vessel  
stenosis. This method is very efficient for treating vessel  
tears which can occur during balloon dilatation. The problems  
with this metallic stents however are that they have proven  
30 to be thrombogenic and can cause an acute thrombotic  
occlusion of the treated blood vessel. On the other hand, it  
appeared that through the implantation of a metal stent in a  
blood vessel, the body can react with an inflammatory  
reaction whereby restenosis within the stent can occur.

35 By covering these endovascular protheses with amphiphilic  
polyurethanes, we succeeded in significantly limiting both  
the problem of thrombogenicity as well as the problem of  
reactive hyperproliferative response.

Amphiphilic polyurethanes were synthesized starting from  
40 amphiphilic polyester diols on the basis of ethylene oxide  
and propylene oxide. By reaction with a diisocyanate and a  
chain lengthener (butanediol), a thermoplastic polyurethane  
is finally obtained. By the appropriate choice of a) the  
polyesterdiol, especially the proportion of  
45 ethyleneoxide/propyleneoxide, and b) the molecular weight  
of the diol, the bio- and blood compatibility can be  
optimized. Furthermore the kind of sterilisation of  
polyurethane-coated devices turned out to be very critical.  
We used certain amounts of gamma radiation which resulted in  
50 the formation of further crossbridging of the polymer leading  
to a more stable and more elastic polymer which is critical  
during the stent deployment. The resulting polymers turned  
out to be very stable when implanted in human or animal  
tissues or blood vessels. Furthermore they did not provoke  
55 any inflammatory reaction.

Furthermore we were able to load these polyurethanes with  
medicines, which were released slowly at the polymer  
implantation side. These medicines are used to further  
decrease the thrombogenicity of the stents (heparin, hirudin,  
60 streptokinase, urokinase, tpa and other anticoagulants) and

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to inhibit the inflammatory reaction caused by the stent  
(corticosteroids, antimitotics, angiopeptin and other  
10 antiinflammatory drugs.) Using methylprednisolone loaded  
polyurethane coated stents we were able to block totally the  
stent restenosis in a pig coronary model.

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#### APPLICATION POSSIBILITES OF THE SYSTEM

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1. Treatment of blood vessel stenosis in humans and animals.

2. Treatment of complications occurring during other  
treatment methods of blood vessel stenosis.

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3. Treatment of complications occurring during diagnostic  
procedures.

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4. Coating of prosteses, wires, and catheters introduced for  
medical purposes.